Interim Guidelines for Lyme Disease Vaccine Use in California for Health Care Providers

Division of Communicable Disease Control
California Department of Health Services

April 1999

A Lyme disease vaccine for use in humans was recently approved by the FDA. Recommendations by the U.S. Public Health Service Advisory Committee on Immunization Practices (ACIP) on the use of this vaccine may not be available for months. In the interim, in anticipation of considerable interest and questions regarding this vaccine, the California Department of Health Services has prepared these guidelines for its use in California. We also review the biology and epidemiology of Lyme disease in California and the existing data on the safety and efficacy of the human Lyme disease vaccine. ***These interim guidelines contain recommendations based on general statewide information. For more specific information on Lyme disease or ticks in local areas, please contact the local health department.***

Summary of Interim Guidelines for Use of Lyme Disease Vaccine in California

1. **Not recommended for routine vaccination anywhere in California**
2. **Should be considered in individuals who have frequent or prolonged contact with natural vegetation (including leaf litter) in tick habitat in areas known to have modest risk (i.e., more than low or no risk) for Lyme Disease (see map)**
3. **Do not deviate from FDA and package insert guidelines for vaccine administration and schedule**
4. **Vaccine is not a substitute for measures to prevent tick bites.**

Lyme disease (LD) is a multi-system syndrome caused by the spirochete *Borrelia burgdorferi*. Most persons reported with LD present with early localized disease characterized by an erythema migrans rash that expands over several days, often with central clearing. Symptoms of early disseminated LD, including fever, myalgia, headache, arthralgia, cranial nerve palsy, and atrioventricular conduction defects, may occur concurrent with, days to weeks after, or in the absence of erythema migrans. If left untreated, some persons with LD can develop oligoarthritis and central nervous system dysfunction. Most cases of LD can be effectively treated with antimicrobials; however, long-term complications may develop if diagnosis and treatment are delayed.

Borrelia burgdorferi is transmitted by ticks of the *Ixodes ricinus* complex. Both the nymphal and adult forms of the tick are capable of transmitting the spirochete. In the upper Midwestern and northeastern United States, the vector is the deer tick (*Ixodes scapularis*); sometimes, > 50% of adult deer ticks in those areas can be infected with *B. burgdorferi*. In the West, the vector is the western black-legged tick (*Ixodes pacificus*). *Ixodes pacificus* ticks have been identified in 56 of California's 58 counties. *Ixodes pacificus* ticks are most common in densely vegetated or wooded areas of the coastal range north of San Francisco, the western Sierra foothills of northern California, and the San Francisco Bay Area including Santa Cruz County; they are less common in the Central Valley and from the Tehachapi Mountains south. The proportion of *I. pacificus* ticks infected with *B. burgdorferi* is comparatively low—based on limited data statewide, approximately 1-2% in adult ticks and 5-6% in nymphs. This low infection rate is due to a separate maintenance cycle involving woodrats and the propensity of immature *I. pacificus* to feed on lizards, which are incompetent reservoirs for the spirochete. A few focal *I. pacificus* populations in northern California have been

identified in which up to 13% of nymphs are infected.

National surveillance for LD was initiated in 1982. The annual number of reported cases has steadily risen from 491 in 1982 to a peak of 16,455 in 1996. Over 85% of the approximately 112,000 cases reported nationwide occurred among residents of the Northeast and Upper Midwest. The states with the highest reported incidence (per 100,000 population) in 1997 included Connecticut (70), Rhode Island (44), New Jersey (25), and New York (18). The reported incidence in California in 1997 was 0.5 per 100,000 population overall, with the incidence being higher for some north coastal counties.

Prevention of LD involves a multi-pronged approach that includes avoidance of tick-infested areas, chemical control of tick populations, environmental management, and personal protective measures. Recently, LYMErix ™ (SmithKline Beecham Pharmaceuticals) became the first LD vaccine approved by the FDA for use in this country; another LD vaccine, ImmuLyme™ (Pasteur Mérieux Connaught), is awaiting FDA approval. Both are recombinant vaccines based on a well-conserved antigen of *B. burgdorferi* known as outer surface protein A (Osp A). The theoretical mechanism of the vaccine is that anti-OspA antibody, ingested during the tick's bloodmeal, will bind with and inactivate spirochetes in the tick's midgut and interrupt spirochetal migration to the salivary gland and transmission to the human host.

Both vaccines are administered in three intramuscular injections: at 0, 1, and 12 months. Field trials demonstrated efficacies of 80-90% in persons who received the full three-dose series. Immunogenicity and efficacy were lower in persons who received only two doses (~50% efficacy) and/or were over 60-65 years of age. Generally, antibodies diminish with time so it is likely that periodic boosters will be necessary. Local reactions such as swelling, redness, and soreness at the inoculation site were reported in approximately 25-30% of vaccinees. Minimal information is currently available about possible delayed adverse effects of vaccination. The relatively brief experience with these vaccines may not have uncovered severe side effects that could become manifest only years later. There have to date been no published safety or efficacy studies of the vaccine in children (<15 years old), adults >70 years old, pregnant women, immunocompromised individuals, or patients with chronic arthritis. Therefore, the vaccine is currently not recommended for individuals in these groups. Safety and efficacy have also not been published using alternative dosage schedules or with simultaneous administration of other vaccines.

Based on current information on vaccine safety and efficacy, and the known epidemiology of LD in California, **LD vaccine is NOT recommended for routine vaccination anywhere in California.** Decision analysis models indicate that routine administration of the LD vaccine is cost-effective only for populations at much higher risk of LD--i.e., in populations with annual incidence greater than 1000 cases per 100,000 population.

Although LD cases have been reported from almost every county in California, based on tick studies and the residences of reported cases of LD to date, there are defined geographic areas in this state with *some* or *modest* risk for LD, relative to the rest of the State where the risk is low or nil. These areas of more than minimal risk include the northern coastal range (*modest* risk), the western Sierra foothills (*some* risk), and the San Francisco Bay Area including Santa Cruz County (*some* risk) (see map). **LD vaccination should be considered in individuals who have frequent or prolonged**

exposure (i.e., actual contact) to natural vegetation (including leaf litter) in wooded, brushy, or overgrown grassy habitats WITHIN geographic areas known to have *modest* risk for LD (see Summary Table)**.** Examples of individuals with prolonged and frequent contact are park rangers and persons working daily in such environments. For individuals with exposure in *modest* risk areas but whose exposures are neither frequent nor prolonged (such as regular weekend hikers who do not usually go off the trails into brushy vegetation), and for individuals with frequent and prolonged exposure but in areas with *some* risk, LD vaccine may be considered; **however, the benefit of vaccination beyond that provided by basic personal protective measures and early diagnosis and treatment of infection is uncertain**. Persons considering LD vaccination should consult with their health care provider about the benefits and potential risks of LD vaccination. Risk should be assessed on an individual basis, considering the density and prevalence of infected *I. pacificus* ticks in the environment, and the potential for person-tick contact. LD vaccine is **NOT** recommended for persons with exposure (frequent or infrequent) to vegetation in low or no risk areas of the State (see map).

Vaccine administration and schedule should not deviate from FDA and package insert guidelines. LYMErix™ (SmithKline Beecham Pharmaceuticals) should be administered intramuscularly as a three-dose series, with the second and third dose given one and twelve months, respectively, after the first dose.

It is important to note that the LD vaccine offers protection against only infection with *B. burgdorferi* and that even this protection is not 100%. There is no evidence yet to suggest that use of the vaccine in California (or elsewhere, for that matter) is of proven benefit beyond measures to prevent tick bites. The decision to vaccinate will depend on an objective evaluation of individual risks for LD and the physician's discussion with individual patients about the risks, benefits, and present limitations of the vaccine. Persons who, after consultation with their physician, elect to receive the vaccine remain at risk, however, for other tick-transmitted diseases known to occur in California, most especially ehrlichiosis and babesiosis. **LD vaccine is NOT a substitute for measures to prevent tick bites**. Individuals should practice the following personal protective measures as the most effective means of decreasing the risk of all tick-borne diseases: avoid areas with high tick populations, wear appropriate clothing, use repellants, conduct tick checks, and promptly remove any identified ticks.

SUMMARY TABLE OF CALIFORNIA INTERIM GUIDELINES FOR LYME DISEASE VACCINE

Geographic Area of Risk (see map)

Exposure to Tick Habitat	**Modest**	**Some**	**Low or None**
Frequent or prolonged	Vaccine *should be* considered	Vaccine *may be* considered	Vaccine *not* recommended
Occurs but is not frequent or prolonged	Vaccine *may be* considered	Vaccine *not* recommended	Vaccine *not* recommended
Minimal or none	Vaccine *not* recommended	Vaccine *not* recommended	Vaccine *not* recommended

Areas of Lyme Disease Risk in California - 1999

(based on reported human cases and Ixodes tick ecology and infection rate)

Use of Lyme Disease Vaccine in California: Questions and Answers

How does the Lyme disease (LD) vaccine work?

After a person is vaccinated, the vaccine stimulates the individual's immune system to produce antibodies against a specific protein found on the LD bacteria called "Outer surface protein A", or OspA. When a vaccinated individual is bitten, the tick ingests blood containing the anti-OspA antibodies, which then bind and inactivate the LD bacteria, effectively preventing transmission of the bacteria to the vaccinated individual.

How is the vaccine given?

The LD vaccine is administered as a series of three injections into the muscle; the second dose is given one month, and the third dose twelve months, after the first dose.

How good is the vaccine?

Testing of the LD vaccines was conducted among approximately 20,000 individuals residing in areas of the northeastern and upper Midwestern U.S. where the risk of LD is much higher than in California. The vaccine was shown to be 50% effective after 2 doses, and 80-90% effective after the third dose in preventing LD during the one-year follow up period. The effectiveness was lower among persons aged 60 and older.

After I get the first series of three shots, how often do I need to receive a booster?

There are preliminary data that the antibodies from vaccination decline rather rapidly, therefore booster doses of vaccine may be needed (perhaps yearly) to maintain adequate protection. However, there is no recommendation for booster at this time.

Are there any side effects to the LD vaccine?

In the vaccine testing phase, 25-30% of vaccine recipients experienced a local reaction--pain, swelling, tenderness at the injection site--within the first 30 days following vaccination. Approximately 20% experienced mild headache, fever, or muscle and joint ache during this same time period. Since this is a new vaccine, the potential for late, long-term complications of vaccination is unknown.

Once I have been vaccinated, is it then safe to engage in activities in areas where there are ticks?

It is important to remember that maximum LD protection is not conferred until after the third vaccine dose, given one year after the first. Even then, the expected protection is less than 100%. Also, the LD vaccine provides no protection against other diseases that ticks can transmit. Therefore, even vaccinated persons should continue to use personal protective measures, including wearing proper clothing, applying insect repellants, performing whole-body tick checks, and promptly removing attached ticks. These measures should be practiced daily when in tick-infested areas.

When should LD vaccine be considered in California?

LD vaccine is not recommended for routine vaccination anywhere in California because the risk for LD is much lower in this State compared to the upper Midwestern and northeastern states. However, within California, there are areas of *modest* risk for LD, particularly the northern coastal range, and areas of *some* risk such as the western Sierra foothills and the San Francisco Bay area (see map). In the areas of *modest* risk, LD vaccine should be considered in individuals who have frequent or prolonged contact with natural vegetation (including leaf litter). Examples of individuals with prolonged and frequent contact are park rangers and persons working daily in such environments. For individuals with exposure in those areas but whose exposures are neither frequent nor prolonged (such as regular weekend hikers who usually go off the trails into brushy vegetation), and for individuals with frequent and prolonged exposure but in areas with *some* risk, LD vaccine may be considered; but there is no data to support that the vaccine is more beneficial than personal protective measures in those situations. In areas of low or no risk and in situations where minimal or no exposure occurs, LD vaccine is not recommended.

My family is planning a vacation to an area where ticks are prevalent. Should we be vaccinated for Lyme disease?

Vaccination is not generally recommended for persons who occasionally travel to areas where LD is prevalent. Maximum protection from the LD vaccine is conferred only after completion of the third dose, which is administered one year after the initial two doses. In this situation, there is no data to prove that the vaccine is more beneficial than personal protective measures described above. Contact the local health department in the areas you plan to visit to determine if Lyme disease is a serious risk in these areas.

I believe my family may be at risk of getting Lyme disease. What's the age at which a person may be vaccinated?

Persons less than 15 years old or older than 70 were not included in the vaccine field trials, thus information on the safety and efficacy of the vaccine in these age groups is unavailable. The vaccine is therefore not recommended for use in these persons.

For what other persons is the vaccine not recommended for use at this time?

1) Women who were pregnant or planning to become pregnant were specifically excluded from the vaccine field trials, so information on the safety of the vaccine for pregnant women and the developing fetus is unavailable.

2) Individuals with decreased immune function (from illness or chemotherapy), people who have active or chronic arthritis, heart block or using pacemakers were also excluded from the vaccine trials, so there is no safety data for the use of vaccine in these persons.

My family enjoys hiking and camping in the mountains and foothills each summer and we

frequently pull ticks off our clothing. Should we consider getting vaccinated for Lyme disease?

Vaccination is not routinely recommended for persons who occasionally travel for work or recreation to areas where ticks are present. Infected ticks capable of transmitting the Lyme disease organism have been found in modest numbers in only a few areas of California--notably the northern coastal mountain ranges. In those areas, LD vaccine may be considered for exposure that is neither prolonged nor frequent; however, staying on trails and not brushing against bushes or leaf litter piles would significantly decrease contact with ticks. Personal protective methods such as daily tick checks and prompt removal of attached ticks are still the most effective means of preventing LD and other tick-borne diseases. There is no data that the vaccine is more beneficial than personal protective measures for people who occasionally travel or recreate in areas with LD. Remember that the vaccine is not 100% effective and ticks can transmit other diseases for which the LD vaccine provides no protection.

Should I receive the LD vaccine or not?

Because of the small proportion of infected ticks in California and the low risk of infection to most residents, the California Department of Health Services, in accordance with preliminary national guidelines, does not recommend routine use of the LD vaccine in California residents. However, persons who frequently work outdoors in areas with dense vegetation WITHIN geographic areas of modest risk for LD (notably the northern coastal mountain ranges) should be considered for LD vaccination. These persons should consult with their health care provider about the potential benefits and risks of LD vaccination. Because of limited data on safety and efficacy in some groups, the vaccine is currently not recommended for children (<15 years old), adults >70 years old, pregnant women, individuals with compromised immune system function, or patients with chronic arthritis.

Where can I obtain additional information about LD?

Information regarding the prevalence of ticks and risk of LD in your area can be obtained by contacting your local health department or local mosquito/vector control district. (Consult the Government Pages of your local telephone directory.) Information about LD in California is available from the California Department of Health Services, Division of Communicable Disease Control (Tel: 510-540-2566, or http://www.dhs.ca.gov/ps/dcdc/cm/970401CM.htm). Information on LD throughout the United States can be obtained from the Centers for Disease Control and Prevention, Division of Vector-Borne Infectious Diseases (Tel: 970-221-6400, or http://www.cdc.gov/ncidod/dvbid/lymeinfo.htm).